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METHODS: Information regarding physician-diagnosed nonmalignant lung diseases (asbestosis, asthma, chronic bronchitis/emphysema, pneumonia, and tuberculosis) was obtained at baseline from 17,698 men and women involved in the CARET study, a randomized trial of beta-carotene and lung cancer among heavy smokers (aged 50-69 years) and asbestos-exposed workers (aged 45-69 years). Hazard ratios for developing lung cancer were estimated by use of Cox regression models, after controlling for potential confounding factors, included age, intervention arm, smoking status, duration and frequency of smoking, and gender. Analyses were restricted to former and current smokers.
RESULTS: One-thousand twenty-eight cases of lung cancer (218 with squamous cell carcinoma (SCC)) occurred during an average follow-up of 9.1 years. History of asbestosis, asthma, pneumonia, and tuberculosis was similar between lung cancer cases and controls. In contrast, 18.0% of those who developed lung cancer reported a history of chronic bronchitis/emphysema compared to 12.1% of those who did not develop lung cancer (adjusted HR = 1.4, 95% CI 1.2-1.6). In subgroup analyses, the association between a prior diagnosis of bronchitis/emphysema and lung cancer was stronger for those with SCC (HR = 1.7, 95% CI 1.3-2.4), and among those with SCC diagnosed before age 65 years (HR = 2.9, 95% CI 1.7-5.0).
CONCLUSION: Smokers with a history of chronic bronchitis/emphysema may be at higher risk of developing lung cancer, independent of their smoking history.

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P015
CYP1A1 (I462V) AND _NQO1 (P187S)_ POLYMORPHISMS AND COLORECTAL ADENOMA

Lifang Hou[1], Wen-Yi Huang[1], Joel Weissfeld[2], John Gohagan[3], Richard B Hayes[1], Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institute of Health, DHHS, Rockville, MD

PURPOSE: Tobacco use is a risk factor for colorectal adenomas, which are precursors of colorectal cancer. *NQO1* and *CYP1A1* are genes involved in tobacco carcinogen metabolism and polymorphic variants in these genes are suspected to alter tobacco-associated risks for colorectal tumors. We investigated the association of *CYP1A1 (I462V)* and *NQO1 (P187S)* gene polymorphisms with the occurrence and pathological characteristics of colorectal adenomas.
METHODS: We studied 778 cases with large (>1 cm) or histologically advanced (high-grade dysplasia, or villous elements) left-sided adenoma and 788 gender- and ethnicity-matched, poly-free (left-sided) controls in the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Screening Trial. All subjects provided a blood sample and underwent sigmoidoscopy screening with follow-up endoscopy, if indicated. Odds ratios (ORs) and 95% confidence interval (CIs) were calculated using logistic regression models. Multinomial (polytomous) logistic regression models were used to assess risk for colorectal adenoma sub-groups.
RESULTS: Subjects having the valine (minor) variant in *CYP1A1 (I462V)* [OR = 1.0, 95%CI = 0.6-1.6] or the serine (minor) variant in *NQO1 (P187S)* [OR = 1.2, 95%CI = 0.95-1.5] were not at increased risk for colorectal adenoma. Subjects who carried the minor variant in both genes were at excess risk (OR = 1.9, 95%CI = 1.0-3.6), with the excess noted in smokers (OR = 3.1, 95%CI = 1.2-7.9), but not in non-smokers (OR = 1.1). The excess risks associated with this combined genotype in *CYP1A1* and *NQO1* were particularly strong for subjects with adenomas of advanced histology (OR = 2.6, 95%CI = 1.2-3.9) or with multiple adenomas (OR = 4.1, 95%CI = 2.0-8.6).
CONCLUSION: The combination of *CYP1A1 (I462V)* and *NQO1 (P187S)* minor variant polymorphisms increase risk for colorectal adenoma, suggesting a role for these genes in colorectal carcinogenesis, possibly related to tobacco-related carcinogenesis.

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P016S
ENVIRONMENTAL TOBACCO SMOKING AND SMOKING-RELATED SUSCEPTIBILITY GENES FOR THE RISK OF ESOPHAGEAL, STOMACH, AND LIVER CANCERS

NC You, LN Mu, SZ Yu, QW Jiang, W Cao, XF Zhou, BG Ding, RH Wang, L Cai, ZF Zhang, UCLA School of Public Health, Los Angeles, CA, and Fudan University School of Public Health, Shanghai, China

PURPOSE: Several studies found that expose to ETS may increase the risk of lung cancer in non-smokers; however, very few studies have been conducted for other active tobacco smoking-related cancers. Our objectives are to use a population-based case-control study design to better understand the toxic mechanisms of ETS as well as tobacco smoking-related genes (GSTM1 & GSTT1) and to explore potential interactions between them on the risk of esophageal, stomach and liver cancers in non-smokers. Our hypotheses are ETS exposure, null type of GSTM1 and GSTT1 may increase the risk of these three cancers, and there is gene-environmental interaction between them.
METHODS: We conducted a population-based case-control study based on non-smokers, including 84 esophageal cancer, 85 stomach cancer and 79 liver cancer incident cases and 204 healthy population controls in Taixing City, China from March 1, 2000 to August 31, 2000. ETS and confounders information was collected by face-to-face interview by trained interviewers using a standard questionnaire. GSTM1 and GSTT1 were assayed by PCR techniques. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression models in SAS.
RESULTS: We found ETS is associated with increased risk of esophageal cancer (OR = 1.72 & 95% CI = 1.0-3.1), and borderline associated with increased risk of stomach (OR = 1.33 & 95% CI = 0.8-2.3) and liver cancers (OR = 1.13 & 95% CI = 0.6-1.9). There are dose-response relations between total years of ETS exposure and the risk of these three cancers. Potential gene-environment interactions were suggested between GSTM1 polymorphisms and ETS on the risk of these three cancers. The effect of ETS is stronger on the people with normal GSTM1 genotype.
CONCLUSION: ETS exposure may increase the risk of esophageal, stomach and liver cancers, and GSTM1 may modify the effect of ETS on these three upper digestive system cancers.

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